



| | | CDR2 | FR3 |
|------|--------------------|---------|----------------------------------|
| | | 5 | 6 7 8 |
| AHM | (SEQ ID NO: 130) | 0123456 | 78901234567890123456789012345678 |
| HuSG | I (SEQ ID NO: 131) | SASNRYT | GVPDRITGSGSGTDFTFTISSVQAEDLALYYC |
| REI | (SEQ ID NO: 132) | | GVPSRFSGSGSGTDFTLTITSSLPEDFATYYC |
| RVLa | (SEQ ID NO: 133) | ----- | GVPSRFSGSGSGTDFTFTITSSLPEDIATYYC |
| RVLb | (SEQ ID NO: 134) | ----- | -----Y----- |

| | | CDR3 | FR4 |
|------|--------------------|-----------|------------|
| | | 9 | 10 |
| AHM | (SEQ ID NO: 130) | 901234567 | 8901234567 |
| HuSG | I (SEQ ID NO: 131) | QQHYSTPFT | FGSGTKLEIK |
| REI | (SEQ ID NO: 132) | | FGQGTKVEIK |
| RVLa | (SEQ ID NO: 133) | ----- | FGQGTKVEIK |
| RVLb | (SEQ ID NO: 134) | ----- | ----- |

On page 62, delete Table 4, and replace this with the following in accordance with 37 C.F.R. § 1.121. A marked up version showing changes is attached:

Table 4

The amino acid sequence of the H chain V region (1)

| | | FRI | CDR1 | FR2 |
|-------|------------------|--------------------------------|-------|----------------|
| | | 1 2 3 | 4 | 4 |
| AHM | (SEQ ID NO: 135) | 123456789012345678901234567890 | 12345 | 67890123456789 |
| HuSGI | (SEQ ID NO: 136) | QVQLQQSGAELARPGASVKLSCKASGYTFT | PYWMQ | WVKQRPGQGLEWIG |
| HG3 | (SEQ ID NO: 137) | EVQLVQSGADVKKPGXSXVVSCKASGYTFS | | WVRQAPGXGLDWVG |
| RVHa | (SEQ ID NO: 138) | QVQLVQSGAEVKKPGASVKVSCKASGYTFN | | WVRQAPGQGLEWMG |
| RVHb | (SEQ ID NO: 139) | -----T | ----- | ----- |
| RVHc | (SEQ ID NO: 140) | -----T | ----- | ----- |
| RVHd | (SEQ ID NO: 141) | -----T | ----- | ----- |
| RVHe | (SEQ ID NO: 142) | -----T | ----- | ----- |
| RVHf | (SEQ ID NO: 143) | -----T | ----- | ----- |
| RVHg | (SEQ ID NO: 144) | -----T | ----- | -----R----- |
| RVHh | (SEQ ID NO: 145) | -----T | ----- | ----- |
| RVHi | (SEQ ID NO: 146) | -----T | ----- | ----- |
| RVHj | (SEQ ID NO: 147) | -----T | ----- | ----- |
| RVHk | (SEQ ID NO: 148) | -----T | ----- | ----- |
| RVHl | (SEQ ID NO: 149) | -----T | ----- | ----- |
| RVHm | (SEQ ID NO: 150) | -----T | ----- | ----- |
| RVHn | (SEQ ID NO: 151) | -----T | ----- | ----- |
| RVHo | (SEQ ID NO: 152) | -----T | ----- | ----- |
| RVHp | (SEQ ID NO: 153) | -----T | ----- | ----- |
| RVHq | (SEQ ID NO: 154) | -----T | ----- | ----- |
| RVHr | (SEQ ID NO: 155) | -----T | ----- | ----- |

Table 5

On page 63, delete Table 5, and replace this with the following in accordance with 37 C.F.R. § 1.121. A marked up version showing changes is attached:

| | CDR2 | FR3 |
|------------------------|-------------------|-----------------------------------|
| | 5 6 | 7 8 9 |
| | 012A3456789012345 | 67890123456789012ABC345678901234 |
| AHM (SEQ ID NO: 156) | SIFPGDGDTRYSQKFKG | KATLTADKSSSTAYMQLSILAFEDSAVYYCAR |
| HuSGI (SEQ ID NO: 157) | | RVXTXDXSXNTAYMELSSLRSEDVAVYYCAR |
| HG3 (SEQ ID NO: 158) | | RVTMTTRDTSTSTVYMELESLRSEDVAVYYCAR |
| RVHa (SEQ ID NO: 159) | ----- | -----A----- |
| RVHb (SEQ ID NO: 160) | ----- | K-----A----- |
| RVHc (SEQ ID NO: 161) | ----- | -----A-K----- |
| RVHd (SEQ ID NO: 162) | ----- | K-----A-K----- |
| RVHe (SEQ ID NO: 163) | ----- | -A-L-A----- |
| RVHf (SEQ ID NO: 164) | ----- | -A-L-A---S--A----- |
| RVHg (SEQ ID NO: 165) | ----- | -----A----- |
| RVHh (SEQ ID NO: 166) | ----- | K---A---S--A----- |
| RVHi (SEQ ID NO: 167) | ----- | K---A---S--A-----AF----- |
| RVHj (SEQ ID NO: 168) | ----- | KA-L-A---S--A----- |
| RVHk (SEQ ID NO: 169) | ----- | K---A---S==A--Q----- |
| RVHl (SEQ ID NO: 170) | ----- | K---A---S--A--Q--1----- |
| RVHm (SEQ ID NO: 171) | ----- | K---A---S--A--Q--1---S----- |
| RVHn (SEQ ID NO: 172) | ----- | K---A---S--A---1----- |
| RVHo (SEQ ID NO: 173) | ----- | K---A---S--A-----S----- |
| RVHp (SEQ ID NO: 174) | ----- | -----A-----A----- |
| RVHq (SEQ ID NO: 175) | ----- | -----A--S----- |
| RVHr (SEQ ID NO: 176) | ----- | -----A-K-----A----- |

On page 64, delete Table 6, and replace this with the following in accordance with 37 C.F.R. § 1.121. A marked up version showing changes is attached:

Table 6

| | CDR3 | FR4 |
|------------------------|-------------|-------------|
| | 10 | 11 |
| | 57890ABJK12 | 34567890123 |
| AHM (SEQ ID NO: 177) | GLRRGGYYFDY | WGQGTTLTVSS |
| HuSGI (SEQ ID NO: 178) | ----- | WGQGTTLTVSS |
| JH6 (SEQ ID NO: 179) | ----- | WGQGTTLTVSS |
| RVHa (SEQ ID NO: 180) | ----- | ----- |
| RVHb (SEQ ID NO: 181) | ----- | ----- |
| RVHc (SEQ ID NO: 182) | ----- | ----- |
| RVHd (SEQ ID NO: 183) | ----- | ----- |
| RVHe (SEQ ID NO: 184) | ----- | ----- |
| RVHf (SEQ ID NO: 185) | ----- | ----- |
| RVHg (SEQ ID NO: 186) | ----- | ----- |
| RVHh (SEQ ID NO: 187) | ----- | ----- |
| RVHi (SEQ ID NO: 188) | ----- | ----- |
| RVHj (SEQ ID NO: 189) | ----- | ----- |
| RVHk (SEQ ID NO: 190) | ----- | ----- |
| RVHl (SEQ ID NO: 191) | ----- | ----- |
| RVHm (SEQ ID NO: 192) | ----- | ----- |

B4

| | | | |
|------|------------------|-------|-------|
| RVHn | (SEQ ID NO: 193) | ----- | ----- |
| RVHo | (SEQ ID NO: 194) | ----- | ----- |
| RVHp | (SEQ ID NO: 195) | ----- | ----- |
| RVHq | (SEQ ID NO: 196) | ----- | ----- |
| RVHr | (SEQ ID NO: 197) | ----- | ----- |

On page 72, delete Table Design of V Region of Natural Humanized Antibody, and replace this with the following in accordance with 37 C.F.R. § 1.121. A marked up version showing changes is attached:

Design of V region of Natural Humanized Antibody

A) L chain

| | FR1 | 1 | 2 | CDR1 | 3 | FR2 | 4 | CDR2 | 5 |
|--|-------------------------|---|---|-------------|---|-----------------|---|---------|---|
| HM1.24 (SEQ ID NO: 130) | 12345678901234567890123 | | | 45678901234 | | 567890123456789 | | 0123456 | |
| HuSG I (SEQ ID NO: 131) | DIVMTQSHKFMSTSVGDRVSITC | | | KASQDVNTAVA | | WYQQKPGQSPKLLIY | | SASNRYT | |
| REI (SEQ ID NO: 132) | DIQMTQSPSSLSASVGDRVTITC | | | | | WYQQKPGKAPKLLIY | | | |
| Primary design (RVLa (SEQ ID NO: 133)) | DIQMTQSPSSLSASVGDRVTITC | | | | | WYQQKPGKAPKLLIY | | | |
| Secondary design (SEQ ID NO: 133) | ----- | | | ----- | | ----- | | ----- | |

| | FR3 | 6 | 7 | 8 | 9 | CDR1 | 10 | FR2 |
|--|----------------------------------|---|---|---|---|-------------|----|------------|
| HM1.24 (SEQ ID NO: 130) | 78901234567890123456789012345678 | | | | | 901234567VA | | 8901234567 |
| HuSG I (SEQ ID NO: 131) | GVPRITGSGSGTDFFTISSVQAEIDLALYYC | | | | | QOHYSTPFT | | FGSGTKLEIK |
| REI (SEQ ID NO: 132) | GVPSRFGSGSGTDFTLTISLQPEDFATYYC | | | | | | | FGQGTKVEIK |
| Primary design (RVLa (SEQ ID NO: 133)) | GVPSRFGSGSGTDFTLTISLQPEDFATYYC | | | | | | | FGQGTKVEIK |
| Secondary design (SEQ ID NO: 133) | ----- | | | | | ----- | | ----- |

On page 73, delete Table Design of V Region of Natural Humanized Antibody, and replace this with the following in accordance with 37 C.F.R. § 1.121. A marked up version showing changes is attached:

Design of V region of Natural Humanized Antibody

B) H chain

| | FR1 | CDR1 | FR2 | CDR2 |
|---|--------------------------------|-------|-----------------|-------------------|
| HM1.24 (SEQ ID NO: 198) | 123456789012345678901234567890 | 12345 | 67890123456789 | 012A3456789012345 |
| HuSG I (SEQ ID NO: 199) | QVQLQSGAELARPGASVKLSCKASGYTFT | PYWMQ | WVKQRPGQGLEWIG | SIFPGDTRYSQKFKG |
| HG3 (SEQ ID NO: 200) | EVQLVQSGADVKKPGXSVXVCKASGYTFS | --- | WVRQAPGXLGDLWVG | --- |
| Primary design (RVHr (SEQ ID NO: 201) | QVQLVQSGAEVKKPGASVKVCKASGYTFN | --- | WVRQAPGQGLEWMG | --- |
| Secondary design (2 nd RVH) (SEQ ID NO: 202) | -----T | --- | --- | --- |

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| | FR3 | CDR3 | FR2 |
|---|------------------------------------|-------------|-------------|
| HM1.24 (SEQ ID NO: 198) | 67890123456789012ABC345678901234 | 57890ABJK12 | 34567890123 |
| HuSG I (SEQ ID NO: 199) | KATLTADKSSSTAYMQLSILAFEDSAVYICAR | GLRRGGYIFDY | WGQGTTLTVSS |
| HG3 (SEQ ID NO: 200) | RVTXTXDXSXNTAYMELSSLRSEDTAVYICAR | --- | WGQGTTLTVSS |
| Primary design (RVHr (SEQ ID NO: 201) | RVTMTTRDTSTSTVYMEELSSLRSEDTAVYICAR | --- | --- |
| Secondary design (2 nd RVH) (SEQ ID NO: 202) | -----A-K---A | --- | --- |
| | ---I-A-K---A | --- | --- |

On page 74, delete line 23 and replace this with the following in accordance with 37 C.F.R. § 1.121. A marked up version showing changes is attached:

b1
FR3 of primary design antibody (SEQ ID NO: 203)